

JC17 Rec'd PCT/PTO 31 MAR 2005

Amendments to the Claims

The current status of all claims is listed below and supercedes all previous lists of claims.

Please cancel claims 1-148 without prejudice to the applicants' right to reinstate those claims or pursue the subject matter of the cancelled claims in a further application.

1-148. (Cancelled)

Please add claims 149-196 as follows.

149 (New). A method of treating or preventing a disease or a symptom of a disease in an animal comprising administering to said animal an amount of a composition comprising a non-pathogenic, insect-specific virus effective to treat or prevent the disease or disease symptom in said animal.

150 (New). The method of claim 149, wherein the composition comprising a non-pathogenic, insect-specific virus is effective at a concentration of less than about 500,000 PFU or about 500,000 PFU Equivalents to cause cell death in greater than about 50% of the contacted cells in an *in vitro* assay.

151 (New). The method of claim 149, wherein the insect-specific virus is a virus of the Baculaviridae family.

152 (New). The method of claim 151, wherein the Baculaviridae virus is a granulosis virus or a nucleopolyhedrosis virus.

153 (New). The method of claim 152, wherein the nucleopolyhedrosis virus is *Autographa californica* nucleopolyhedrosis virus.

154 (New). The method of claim 149 wherein the disease is cancer or an infectious disease, or a symptom of cancer or an infectious disease.

155 (New). The method of claim 154 wherein the cancer is selected from the group consisting of lung, breast, prostate, colon, gastric, pancreatic, renal, or skin cancer.

156 (New). The method of claim 154 wherein the infectious disease is selected from the group consisting of HIV, West Nile virus, hepatitis A, B, C, small pox, tuberculosis, Vesicular Stomatitis Virus, Respiratory Syncytial Virus, human papilloma virus, SARS, influenza, Ebola, viral meningitis, herpes, anthrax or lyme disease.

157 (New). The method of claim 154 wherein the symptom of cancer is selected from the group consisting of tumor growth, abnormal cell growth, metastasis, angiogenesis, cell death, cell invasiveness, weight loss, bleeding, difficulty in breathing, bone fractures, compromised immune system or fatigue.

158 (New). The method of claim 149 further comprising:

- (a) inactivating the non-pathogenic, insect-specific virus by adding trioxalen to the non-pathogenic virus at a concentration between about 5-10 µg/ml and illuminating said non-pathogenic, insect-specific virus with UV at about 365 nm and about 6W for about 15 minutes;
- (b) formulating the inactivated non-pathogenic, insect-specific virus into a pharmaceutical composition; and
- (c) administering the pharmaceutical composition to the subject.

159 (New). The method of claim 149 wherein the non-pathogenic, insect-specific virus is a virus of the Baculaviridae family.

160 (New). The method of claim 149, wherein said composition comprising a non-pathogenic, insect-specific virus is effective at a concentration of less than about 500,000 PFU or about 500,000 PFU equivalents to prevent cell growth in greater than about 50% of the contacted cells in an *in vitro* assay.

161 (New). The method of claim 149, wherein the composition is administered intratumorally and/or peritumorally.

162 (New). The method of claim 149, wherein the animal is a human.

163 (New). The method of claim 149, wherein the non-pathogenic, insect-specific virus is an inactivated virus, a viral particle, a virosome, a Virus Like Particle, a viral occlusion body, or a viral component.

164 (New). The method of claim 163, wherein the viral component comprises at least two viral proteins.

165 (New). The method of claim 149, wherein the non-pathogenic, insect-specific virus comprises gp64.

166 (New). The method of claim 163, wherein the viral component comprises one or more of a nucleic acid, a lipid or a carbohydrate.

167 (New). The method of claim 149, wherein the non-pathogenic, insect-specific virus is an inactivated virus.

168 (New). The method of claim 167, wherein the inactivation is heat-inactivation, chemical inactivation, or UV inactivation, or a combination thereof.

169 (New). The method of claim 167 wherein said inactivation is psoralen inactivation, UV inactivation, or a combination thereof.

170 (New). The method of claim 149, wherein the composition is co-administered with another agent, wherein said agent is a chemotherapeutic, an anti-cancer drug, a vaccine, or combinations thereof.

171 (New). A method of inducing an immune response in an animal comprising administering to said animal an amount of a composition comprising an inactive non-pathogenic, insect-specific virus effective to induce an immune response in said animal.

172 (New). The method of claim 171, wherein said immune response protects against infectious disease.

173 (New). The method of claim 171, wherein said immune response protects against cancer.

174 (New). The method of claim 171, wherein said immune response induces a T-cell memory response.

175 (New). The method of claim 171, wherein said immune response promotes dendritic cell maturation.

176 (New). A method of causing cell death in a cell comprising administering a composition comprising an amount of a non-pathogenic, insect-specific virus to said cell effective to cause cell death in said cell.

177 (New). The method of claim 176, wherein said composition comprising a non-pathogenic, insect-specific virus is effective at a concentration of less than about 500,000 PFU or about 500,000 PFU Equivalents to cause cell death in greater than about 50% of the contacted cells in an *in vitro* assay.

178 (New). A method of causing cell death in a population of cells comprising contacting a composition comprising an amount of a non-pathogenic, insect-specific virus to a portion of said population of cells effective to cause cell death in said population of cells.

179 (New). The method of claim 178 wherein said portion of said population of cells is no more than about 20% of said population.

180 (New). The method of claim 178 wherein the population of cells comprises peripheral blood cells, tumor cells, NK cells or macrophages.

181 (New). The method of claim 171, wherein the insect-specific virus is a virus of Baculaviridae family.

182 (New). The method of claim 171, wherein the non-pathogenic, insect-specific virus is an inactivated virus.

183 (New). A method of predicting *in vivo* anti-tumor activity of a compound comprising:
a) contacting the compound with tumor cells and peripheral blood mononuclear cells; and
b) measuring cell death of said tumor cells;

wherein compounds that cause cell death of contacted tumor cells are predicted to be active *in vivo*.

184 (New). The method of claim 183 wherein said compound is an inactivated virus, a viral particle, a virosome, a Virus Like Particle, a viral occlusion body, or a viral component.

- 185 (New). The method of claim 183 wherein said compound is derived from the Baculoviridae family.
- 186 (New). The method of claim 183 wherein said compound is an insect specific virus.
- 187 (New). The method of claim 183, wherein said tumor cells are A549 cells, 3LL-HM cells, 4T1 cells, MT901 cells, MAT BIII cells, B16 melanoma cells or MG-63 cells.
- 188 (New). A composition comprising a non-pathogenic, insect-specific virus and a pharmaceutically acceptable carrier.
- 189 (New). The composition of claim 188, wherein said non-pathogenic, insect-specific virus is inactivated using two or more methods selected from the group consisting of genetic inactivation, chemical inactivation, photochemical inactivation, UV-light inactivation, heat inactivation, or radiological inactivation, further comprising at least one PBMC.
- 190 (New). A composition comprising an inactivated non-pathogenic, insect-specific virus, at least one antigen, wherein the antigen is distinct from the inactivated non-pathogenic, insect-specific virus, at least one adjuvant, and a pharmaceutically acceptable carrier
- 191 (New). A composition comprising an adjuvant composition, said adjuvant composition comprising an inactivated non-pathogenic, insect-specific virus, at least one antigen, wherein said antigen is distinct from the adjuvant composition, and further wherein said immunostimulating composition is capable of increasing the immune response to the antigen.
- 192 (New). A composition comprising a non-pathogenic, insect-specific virus, one or more peripheral blood mononuclear cells (PBMCs), and a pharmaceutically acceptable carrier.
- 193 (New). The composition of claim 188, wherein the insect-specific virus is a virus of Baculaviridae family.
- 194 (New). The composition of claim 188, wherein the non-pathogenic, insect-specific virus is an inactivated virus.

195 (New). A process for preparing an anti-cancer or anti-infectious disease composition comprising a non-pathogenic, insect-specific virus, said process comprising:

(a) exposing the non-pathogenic, insect-specific virus to a first inactivator effective to inactivate an active virus;

(b) exposing the non-pathogenic, insect-specific virus to a second inactivator effective to inactivate an active virus;

(c) combining said non-pathogenic, insect-specific virus with one or more pharmaceutically acceptable carriers or excipients; and

(d) confirming inactivity of non-pathogenic, insect-specific virus in an in vitro assay.

196 (New). The process of claim 195, wherein the insect-specific virus is a virus of the Baculaviridae family.